Listing of Claims

1. (original) A combination comprising a cyclooxygenase-2 selective inhibitor in a first amount and a topoisomerase II inhibitor in a second amount, wherein said first amount together with said second amount comprises a therapeutically effective amount for treatment of neoplasia or a neoplasia related disorder, and wherein the cyclooxygenase-2 selective inhibitor is a compound of formula

or an isomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein:

R²⁷ is methyl, ethyl or propyl;

R²⁸ is chloro or fluoro;

R²⁹ is hydrogen, fluoro or methyl;

R³⁰ is hydrogen, fluoro, chloro, methyl, ethyl, methoxy, ethoxy or hydroxy;

R³¹ is hydrogen, fluoro or methyl; and

 R^{32} is chloro, fluoro, trifluoromethyl, methyl or ethyl; provided that R^{28} , R^{29} , R^{31} and R^{32} are not all fluoro when R^{27} is ethyl and R^{30} is hydrogen.

2. (original) The combination of Claim 1 wherein the COX-2 selective inhibitor is lumiracoxib.

- 3. (currently amended) The combination of Claim 1 or Claim 2 wherein the topoisomerase II inhibitor is selected from the group consisting of aclarubicin, amonafide, amrubicin, amsacrine, annamycin, 6,9-bis[(2-aminoethyl)amino]-benz[g]isoquinoline-5,10-dione, 1,11-dichloro6-[2-(diethylamino)ethyl]-12,13-dihydro-12-(4-O-methyl-β-D-glucopyranosyl)-5H-indolo[2,3-a] pyrrolo[3,4-c]carbazole-5,7(6H)-dione, crisnatol, daunorubicin, doxorubicin, epirubicin, etoposide, galarubicin, idarubicin, iododoxorubicin, 10-[[6-deoxy-2-O-(6-deoxy-3-O-methyl-α-D-galactopyranosyl)-3,4-O-[(S)-phenylmethylene]-β-D-galactopyranosyl]oxy]-5,12-dihydro-1-methyl-5,12-dioxobenzo[h][1]benzopyrano[5,4,3-cde][1] benzopyran-6-yl ester-3-ethoxypropanoic acid, 8-ethyl-7,8,9,10-tetrahydro-1,6,7,8,11-pentahydroxy-10-[[2,3,6-trideoxy-3-(4-morpholinyl)-α-L-lyxo-hexopyranosyl]oxy]-5,12-naphthacenedione, (7S,9S)-7-[[4-O-(3-amino2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)-2,6-dideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,9,11-trihydroxy-9-(hydroxyacetyl)-5,12-naphthacenedione, merbarone, mitoxantrone, nemorubicin, pirarubicin, N-[2-(dimethylamino) ethyl]-9-hydroxy-5,6-dimethyl-6H-pyrido[4,3-b]carbazole-1-carboxamide, subozoxane, teniposide and valrubicin.
- 4. (currently amended) The combination of Claim 1 or Claim 2 wherein the topoisomerase II inhibitor is selected from the group consisting of doxorubicin, epirubicin and idarubicin.
- 5. (currently amended) The combination of <u>Claim 1</u> any of <u>Claims 1 to 4</u> wherein the cyclooxygenase-2 selective inhibitor and the topoisomerase II inhibitor are administered substantially simultaneously.
- 6. (currently amended) The combination of <u>Claim 1</u> any of <u>Claims 1 to 4</u> wherein the cyclooxygenase-2 selective inhibitor and the topoisomerase II inhibitor are administered sequentially.
- 7. (currently amended) A method for treating a Use of a combination of any of Claims 1 to 4 in manufacture of a medicament for treatment of neoplasia or a neoplasia

related disorder in a mammal in need of such treatment, the method comprising

administering to the mammal a therapeutically effective amount of a topoisomerase II

inhibitor and a cyclooxygenase-2 selective inhibitor wherein the cyclooxygenase-2 selective
inhibitor is a compound of formula

or an isomer, pharmaceutically acceptable salt, ester, or prodrug thereof, wherein:

R²⁷ is methyl, ethyl or propyl;

R²⁸ is chloro or fluoro;

R²⁹ is hydrogen, fluoro or methyl;

R³⁰ is hydrogen, fluoro, chloro, methyl, ethyl, methoxy, ethoxy or hydroxy;

R³¹ is hydrogen, fluoro or methyl; and

R³² is chloro, fluoro, trifluoromethyl, methyl or ethyl;

provided that R²⁸, R²⁹, R³¹ and R³² are not all fluoro when R²⁷ is ethyl and R³⁰ is hydrogen.

8. (currently amended) The <u>method</u> [[use]] of Claim 7 wherein the neoplasia or neoplasia related disorder comprises one or more malignant tumor growths selected from the group consisting of acral lentigenous melanoma, actinic keratoses, acute lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal cancer, anal cancer, anorectal cancer, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary cancer, bone cancer, bone marrow cancer, brain cancer, breast cancer, bronchial cancer, bronchial gland carcinomas, carcinoids,

carcinoma, carcinosarcoma, cholangiocarcinoma, chondrocarcinoma, chorioid plexus papilloma/carcinoma, chronic lymphocytic leukemia, chronic myeloid leukemia, clear cell carcinoma, colon cancer, colorectal cancer, connective tissue cancer, cystadenoma, digestive system cancer, duodenum cancer, endocrine system cancer, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, endothelial cell cancer, ependymal cancer, epithelial cell cancer, esophageal cancer, Ewing's sarcoma, eye and orbit cancer, female genital cancer, focal nodular hyperplasia, gallbladder cancer, gastric antrum cancer, gastric fundus cancer, gastrinoma, germ cell tumors, glioblastoma, glucagonoma, heart cancer, hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatobiliary cancer, hepatocellular carcinoma, Hodgkin's disease, ileum cancer, insulinoma, intraepithelial neoplasia, interepithelial squamous cell neoplasia, intrahepatic bile duct cancer, invasive squamous cell carcinoma, jejunum cancer, joint cancer, Kaposi's sarcoma, kidney and renal pelvic cancer, large cell carcinoma, large intestine cancer, larynx cancer, leiomyosarcoma, lentigo maligna melanomas, leukemia, liver cancer, lung cancer, lymphoma, male genital cancer, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal cancer, mesothelial cancer, metastatic carcinoma, mouth cancer, mucoepidermoid carcinoma, multiple myeloma, muscle cancer, nasal tract cancer, nervous system cancer, neuroblastoma, neuroepithelial adenocarcinoma, nodular melanoma, non-epithelial skin cancer, non-Hodgkin's lymphoma, oat cell carcinoma, oligodendroglial cancer, oral cavity cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillary serous adenocarcinoma, penile cancer, pharynx cancer, pituitary tumors, plasmacytoma, prostate cancer, pseudosarcoma, pulmonary blastoma, rectal cancer, renal cell carcinoma, respiratory system cancer, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, sinus cancer, skin cancer, small cell carcinoma, small intestine cancer, smooth muscle cancer, soft tissue cancer, somatostatin-secreting tumor, spine cancer, squamous cell carcinoma, stomach cancer, striated muscle cancer, submesothelial cancer, superficial spreading melanoma, T cell leukemia, testicular cancer, thyroid cancer, tongue cancer, undifferentiated carcinoma, ureter cancer, urethra cancer, urinary bladder cancer, urinary system cancer, uterine cervix cancer, uterine corpus cancer, uveal melanoma, vaginal cancer, verrucous carcinoma, VIPoma, vulva cancer, well differentiated carcinoma and Wilm's tumor.

9. (currently amended) The <u>method</u> [[use]] of Claim 7 wherein the neoplasia or neoplasia related disorder is selected from the group consisting of lung cancer, colorectal cancer, breast cancer, prostate cancer, bladder cancer, ovary cancer, cervical cancer, gastrointestinal cancer and leukemia.